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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/795,927	03/08/2004	Paul B. Fisher	A34694-PCT-USA-A 070050.2	2669

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EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 06/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/795,927	FISHER ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *61-69,74 and 75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *61-69,74 and 75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11-22-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Specification

The abstract of the disclosure is objected to because it does not describe the elected subject matter. Correction is required. See MPEP § 608.01(b).

The description of the drawings is objected to because the description of Fig. 1 should begin FIGURE 1A-E not 1A-C and the second page of Figure 9 is not labeled.

The title of the invention is not descriptive. A new title will be required that is clearly indicative of the invention to which the claims are directed.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reasons: **The nucleic acid sequence in Fig. 1C does not have a SEQ ID NO.** Applicants must file a "Sequence Listing" accompanied by directions to enter the listing into the specification as an amendment. Applicant also must provide statements regarding sameness and new matter with regards to the CRF and the "Sequence Listing." Failure to fully comply with the sequence rules in response to the instant office action will be considered non-responsive.

This application repeats a substantial portion of prior Application No. 09/948227, filed 9-7-01, and adds and claims additional disclosure not presented in the prior application. Since this application names an inventor or inventors named in the prior application, it may constitute a continuation-in-part of the prior application. Should

applicant desire to obtain the benefit of the filing date of the prior application, attention is directed to 35 U.S.C. 120 and 37 CFR 1.78. Claims 61-69 and 74 were filed with the instant application but were not present in parent application 09/948227. Section 5.6 of parent application has three paragraphs on pg 23, lines 11-30, while Section 5.6 the instant application has five paragraphs spanning from pg 22, line 19, through pg 24, line 2. Section 8 on pg 38-40 is not in parent application '227. The new paragraphs in Section 5.6 and new section 8.0 make the instant application a CIP of '227.

The first line of the specification will have to be updated to indicate the instant application is a CIP of parent case 09/948227.

Oath/Declaration

The oath is defective because it states the instant application is a continuation and not a continuation-in-part.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 61-69 and 74-75 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Breadth of claims

Claim 61 is directed toward a transgenic non-human animal whose cells comprise the nucleic acid having the sequence of SEQ ID NO: 3 (human bivalent prostate carcinoma tumor antigen-1 (B-PCTA-1) protein; GenBank Accession No: L78132).

Claim 67 is drawn to a non-human transgenic animal whose cells express a greater level of PCTA-I protein as compared to the level of PCTA-I protein expressed in a non-human non-transgenic animal of the same inbred strain.

Claim 68 is drawn to a non-human transgenic animal having increased human PCTA-I as compared to a non-human non-transgenic animal of the same inbred strain.

Claim 69 is drawn to a non-human transgenic animal whose cells express a greater level of PCTA-I mRNA as compared to the level of PCTA-I mRNA expressed in a non-human non-transgenic animal of the same inbred strain.

Claims 61 encompasses a transgenic non-human animal receiving gene therapy with a vector encoding SEQ ID NO: 3 as well as a transgenic non-human animal made using a transgene comprising SEQ ID NO: 3.

Claim 67 encompasses a transgenic non-human animal made using a transgene comprising any species of PCTA-1. Claim 67 encompasses a transgenic non-human animal receiving gene therapy with a vector encoding any species of PCTA-1 as well as a transgenic non-human animal made using a transgene comprising any species of PCTA-1.

Claim 68 encompasses a transgenic non-human animal expressing a transgene encoding human PCTA-1 as well as any transgenic non-human animal given human PCTA-1.

Claim 69 encompasses a transgenic non-human animal made using a transgene encoding any protein that causes increased levels of PCTA-1 mRNA, a transgene encoding any species of PCTA-1 that causes increased levels of PCTA-1 mRNA or any transgenic non-human transgenic animal given a protein that causes increased expression of PCTA-1 mRNA.

State of the art/unpredictability

The state of the art at the time of filing was that the phenotype of transgenic animals was unpredictable. Examples in the literature aptly demonstrate that even closely related species carrying the same transgene construct can exhibit widely varying phenotypes. For example, several animal models of human diseases have relied on transgenic rats when the development of mouse models was not feasible. Mullins (1990, Nature, Vol. 344, pg 541-544) produced outbred Sprague-Dawley x WKY rats with hypertension caused by expression of a mouse *Ren-2* renin transgene. Hammer (1990, Cell, Vol. 63, pg 1099-1112) described spontaneous inflammatory disease in inbred Fischer and Lewis rats expressing human class I major histocompatibility allele HLA-B27 and human β_2-microglobulin transgenes. Both investigations were preceded by the failure to develop human disease-like symptoms in transgenic mice (Mullins, 1989, EMBO, Vol. 8, pg 4065-4072; Taurog, 1988, J. Immunol., Vol. 141, pg 4020-4023) expressing the same transgenes that successfully caused the desired symptoms

in transgenic rats. Thus, the phenotype resulting from a particular combination of elements (protein, promoter, species of protein, and species of transgenic) was not predictable at the time of filing.

Not only is the phenotype of transgenic animals unpredictable for reasons stated above, the art at the time of filing was such that a number of significant limitation regarding the production of non-mouse transgenic animals existed. Wall (1996, Theriogenology, Vol. 45, pg 57-68) disclosed the unpredictability of transgene behavior due to factors such as position effect and unidentified control elements resulting in a lack of transgene expression or variable expression (paragraph bridging pages 61-62). Ebert (1988, Mol. Endocrinology, Vol. 2, pages 277-283) taught a transgene encoding the human somatotropin gene operably linked to the mouse metallothionein promoter caused different phenotypes in transgenic pigs and mice (pg 277, col. 2, lines 17-27). Overbeek (1994, "Factors affecting transgenic animal production," Transgenic animal technology, pg 96-98) taught that within one litter of transgenic mice, considerable variation in the level of transgene expression occurs between founder animals and causes different phenotypes (pg 96, last paragraph). Mullins (1996, J. Clin. Invest., Vol. 98, pg 1557-1560) taught that non-mouse ES cells capable of providing germline chimeras were not available (pg 1558, col. 1, first paragraph). Therefore, it was unpredictable at the time of filing how to make transgenics other than mice.

B-PCTA-1 is part of the galectin gene family. B-PCTA-1 is referred to as bivalent because it comprises both carbohydrate recognition domains (CRDs). The specification teaches galectins are classified by distinguishing whether the galectin has a single

CRD, two CRD domains separated by a linker, or an unrelated amino-terminal domain liked to a CRD (pg 2, 1st ¶ of specification). Galectins having tandem repeated CRD domains include galectins 4, 6, 8 and 9 (pg 3, 1st ¶). Single CRD galectin 1 and 2 exist as dimmers (pg 3, 2nd ¶). It is based on the discovery that "increased expression of the full-length open reading frame of PCTA-1 suppressed proliferation of tumor cells while expression of PCTA-1 lacking the second CRD-encoding region had the opposite effect (pg 4, last ¶). B-PCTA-1 can be produced using a nucleic acid as set forth in GenBank Accession No: L78132, SEQ ID NO: 3 from residues 54-1004 (pg 12, 3rd ¶). The B-PCTA-1 protein is SEQ ID NO: 6, Fig. 10.

Gopalkrishnan (Oncogene, 2000, Vol. 19, pg 4405-4416) taught the precise biological functions for the galectin family as a whole, or for individual members has been elusive. PCTA-1 (closely related to rat and human galectin-8) was identified as a surface marker for prostate carcinoma. Overexpression of full length PCTA-1 inhibited growth of tumor cells *in vitro*. This observation is counter-intuitive to what one of skill would have expected of a potential oncogene (pg 4414, beginning of 2nd full ¶). The art at the time of filing did not teach the function of PCTA-1 *in vivo*.

Teachings in the specification

Increased expression of the full-length open reading frame of PCTA-1 suppressed proliferation of tumor cells while expression of PCTA-1 lacking the second CRD-encoding region had the opposite effect (pg 4, last ¶).

Applicants made transgenic mice made using a transgene encoding full length human PCTA-1 operably linked to the human elongation factor 1α promoter (paragraph

bridging pg 38-39). Applicants put the transgenic mice through a battery of tests to determine the phenotype and found the transgenics did not have any observable phenotype (pg 39, lines 6-15).

Pg 40, lines 1-4, teaches transgenic mice overexpressing the protein encoded by SEQ ID NO: 3 crossed with TRAMP mice fail to produce detectable tumors as compared to TRAMP mice. Applicants conclude human PCTA-1 has a tumor suppressive effect.

Analysis

While the specification teaches cells transfected with DNA encoding B-PCTA-1 may be used as a model of malignancy, transfection of cells with DNA encoding B-PCTA-1 inhibited tumor formation. Therefore the specification does not teach how to use the animals claimed as models of malignancy.

Applicants made transgenic mice made using a transgene encoding full length human PCTA-1 operably linked to the human elongation factor 1α promoter (paragraph bridging pg 38-39) and put the transgenic mice through a battery of tests to determine the phenotype and found the transgenics did not have any observable phenotype (pg 39, lines 6-15). Accordingly, it would require those of skill undue experimentation to determine the phenotype of the transgenic animal claimed. Without knowing the phenotype of the animal, one of skill would not be able to determine how to use the transgenic animal claimed. Therefore, the specification fails to teach how to use the transgenic animal claimed because it fails to teach the phenotype of the transgenic animal.

Pg 40, lines 1-4, teaches transgenic mice overexpressing the human PCTA-1 protein encoded by SEQ ID NO: 3 crossed with TRAMP mice fail to produce detectable tumors as compared to TRAMP mice. Applicants conclude human PCTA-1 has a tumor suppressive effect. Applicants do not teach how to use the PCTA-1/TRAMP mice for any further research. Nor are any uses for the singly transgenic PCTA-1 mouse readily apparent from such a conclusion. Furthermore, applicants are not claiming the doubly transgenic mouse. The teachings in example 8 do not provide adequate guidance for those of skill to use either the singly transgenic PCTA-1 mouse or the doubly transgenic PCTA-1/TRAMP mouse.

Applicants acknowledge that the normal physiological roles of galectins remain unknown (pg 3, line 1), it was unpredictable whether galectins were stimulatory or inhibitory because some galectins are stimulatory and some cause apoptosis (pg 37, 9-14). The specification does not teach the physiological role of B-PCTA-1 of a normal animal. In addition, different isoforms of B-PCTA-1 are expressed in different amount by a given cell population and possibly within the same cell at all times (pg 28, lines 15-30; pg 31, lines 3-5, "A complete lack of consistency PCTA-1 isoform expression has been observed in a given cell type"). The specification does not teach the function of B-PCTA-1 expression *in vivo* or the phenotype of any animal carrying a B-PCTA-1 transgene. The specification does not provide adequate guidance regarding the phenotype of the transgenic animal claimed such that those of skill would overcome the unpredictability in the art and determine the phenotype of the transgenic claimed.

The specification does not enable one of skill to make a transgenic non-human animal whose cells comprise the nucleic acid sequence of SEQ ID NO: 3 as broadly claimed (claim 61). The claim encompasses administering the nucleic acid sequence of the transgenic non-human animal by gene therapy. However, the specification does not provide any means of providing gene therapy. Without such guidance, it would require one of skill undue experimentation to determine how to make a transgenic non-human animal whose comprise SEQ ID NO: 3 using gene therapy as broadly encompassed by the claim.

The specification does not enable one of skill to make a transgenic non-human animal whose cells express a greater level of any PCTA-1 as broadly claimed (claim 67). The only B-PCTA-1 transgene disclosed in the specification or in the art at the time of filing is the coding region of human PCTA-1 described in SEQ ID NO: 3 from residues 54-1004. The specification does not teach prostate carcinoma tumor antigens in any other species or how to isolate any PCTA-1 from any other species. It would require one of skill undue experimentation to determine whether other B-PCTA-1 exist or how to isolate such proteins. Therefore, one of skill could not cause greater expression of any PCTA-1 as broadly claimed.

The specification does not teach any transgenic having increased human PCTA-1 protein activity (claim 68) other than those having increased activity of the protein encoded by SEQ ID NO: 3. The specification does not teach how any other human PCTA-1 protein other than the one encoded by SEQ ID NO: 3. It would require one of skill undue experimentation to determine whether other human PCTA-1 proteins exist or

how to isolate such proteins. Therefore, one of skill could not cause greater expression of any human PCTA-1 as broadly claimed.

The specification does not teach how to increase human PCTA-1 protein activity (claim 68) other than by making a transgenic non-human animal whose genome comprises a transgene. The claim encompasses administering human PCTA-1 protein to any transgenic non-human animal and then finding a way to increase activity of the protein. No such teachings can be found in the specification and it would require one of skill undue experimentation to determine how to do so. Therefore, one of skill could not cause greater expression of human PCTA-1 in a transgenic non-human animal other than by making a transgenic non-human animal whose genome comprised a nucleic acid sequence encoding human PCTA-1.

The specification does not teach how to increase PCTA-1 mRNA (claim 69) other than by making a transgenic non-human animal whose genome comprises a transgene encoding PCTA-1. The claim encompasses administering a compound that stimulates PCTA-1 expression to any transgenic non-human animal. No such teachings can be found in the specification and it would require one of skill undue experimentation to determine how to do so. Therefore, one of skill could not cause greater PCTA-1 mRNA levels in a transgenic non-human animal other than by making a transgenic non-human animal whose genome comprised a nucleic acid sequence encoding PCTA-1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 61, 62, 67-69, 74 and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kasper (1998, Laboratory Invest., Vol. 78, No. 3, pg 319-333) in view of Su (PNAS, July 1996, Vol. 93, pg 7252-7257).

Kasper taught a transgenic mouse whose genome comprised a transgene comprising rat prostate tumor-specific antigen (probasin) operably linked to a promoter. The transgenic mouse overexpressed probasin; therefore, the mouse had an increased probasin activity and mRNA levels. Kasper did not teach making a mouse whose genome comprised human PCTA-1.

However, Su taught the nucleic acid sequence of SEQ ID NO: 3 (GenBank No: L78132) for human prostate carcinoma tumor antigen-1 (PCTA-1) (pg 7252, col. 2, "Data Deposition" at the bottom of the page).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to make a transgenic mouse whose genome comprised a prostate tumor antigen from a non-mouse species as taught by Kasper, wherein the prostate tumor antigen was the human prostate carcinoma antigen encoded by SEQ ID NO: 3 taught by Su. One of ordinary skill in the art at the time of filing would have been motivated to replace the rat prostate tumor antigen used by Kasper with the human prostate tumor antigen taught by Su to determine the function of PCTA-1 *in vivo*.

The specification teaches transgenic mice comprising SEQ ID NO: 3 did not have altered phenotypes (pg 39, lines 6-18). Therefore, the combined teachings of Kasper and Su are no less than the teachings in the specification.

Thus, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

HomoloGene shows PCTA-1 in humans, mice and rats is now known as LGALS8 (lectin, galactoside-binding, soluble, 8 or galectin 8).

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on 571-272-0735.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

MICHAEL WILSON
PRIMARY EXAMINER